APPLICATION FOR A GOSHCC SURGICAL SCIENTIST PHD STUDENTSHIP

Academic Supervisors
Name: Dr. Andrew Cook
   Dr. Owen Arthurs
ICH Programme/Section: DBC

Clinical Supervisors
Name: Mr Martin Kostolny  GOSH department: Cardiothoracic surgery

1. Title
Micro-structural imaging and analysis of the left ventricular outflow in children with congenital heart malformations to aid surgical repair and design implants.

2. Portfolio summary

Aims:
This proposal aims to use the novel techniques of X-ray Phase-contrast Imaging (XPCI) and Micro-Computed Tomography (MCT) to look in detail at the micro-anatomy of the systemic outflow tract. We will look at specific forms of congenital heart disease that are amenable to surgical repair rather than valve replacement in children and young adults, and are also a potential target for future trans-catheter aortic valve design and implantation (TAVI). Results will be used to inform on, and potentially improve, current surgical techniques used in an extending cohort of children and young adults at GOSH, undergoing this type of surgical repair who will be reviewed as part of this study.

Background:
Surgical repair of the aortic valve and root, as opposed to early valve replacement in infancy or early adulthood, is becoming a more recognised surgical strategy in patients with aortic valve stenosis. Similar strategies are also important in other specific but rarer systemic outflow tract abnormalities. Examples are the arterial switch operation for transposition of the great arteries in whichneo-aortic root dilatation can be problematic; construction of a neo-aortic root in common arterial trunk with abnormal trunk valve; and left ventricular outflow tract obstruction in the setting of ventricular septal defect and aortic arch obstruction. Given these trends, a detailed understanding of the systemic outflow tract, over and above gross anatomy, is warranted in order to develop further both surgical and interventional techniques, such as single versus whole leaflet excision and replacement, enlargement of commissures and debaulking of leaflets and TAVI valve design and implantation.

Imaging prior to surgery is crucial. At GOSH trans-thoracic 3D echocardiography is supplemented with intra-operative echo including trans-oesophageal echo in older patients. CT is generally restricted in young patients at GOSH due to radiation dose, but is used in other centres worldwide and frequently in the setting of TAVI in older patients. Thus imaging is possible but with further understanding of micro-anatomy it may be possible to direct these procedures further to aid surgical repair or intervention.

Both XPCI and MCT are novel techniques that we have been developing in our unit over the past 2-3 years. They allow non-destructive imaging of irreplaceable archival material (HTA licenced Cardiac Archive at ICH), preserving samples for future teaching and research.
XPCI allows imaging of small (fetal & pre-term) whole heart specimens from <1um upwards to whole organ level. MCT allows examination of whole heart specimens from fetal life to adulthood, but at lower resolution (20-30um). From these studies we have shown that XPCI can resolve cardiac structure in super high detail showing the orientation of groups/aggregates of myocytes, the conduction system as well as microvasculature.

We have transferred the same computational methodology the analysis of MCT images of animal hearts from the Royal Vet College and then selected human fetal and postnatal specimens from the ICH Cardiac Archive.

**Proposed methodology to be adopted:**

The proposal will be divided into the following broad workpackages which will be refined as our XPCI and MCT work progresses:

| Workpackage 1 | i. | Review of current literature |
| Workpackage 2 | i. | Morphologic analysis of the systemic outflow tract in aortic valve stenosis, common arterial trunk, transposition, and VSD with systemic outflow tract obstruction in specimens from the HTA Lienced Cardiac Archive at UCLs Institute of Child Health/Cardiovascular Science. Possible addition of further cases from Birmingham’s Children’s Hospital as required. Complete sequential segmental analysis of hearts; Documentation of associated lesions; detailed analysis of the aortic root and valve in terms of leaflet morphology, nodularity, calcification, commissural fusion, interleaflet triangles, sinus and ascending aorta morphology |
| | ii. | Selection of cases suitable for XPCI and MCT imaging |
| Workpackage 3 | i. | Optimisation of protocols for XPCI and MCT analysis of the outflow tract in terms of: Optimal Iodine staining (MCT), analysis of signal to noise ratio of differing tissue components to allow accurately identify fibrous and valvar tissue, arterial wall, conduction tissue, and myocardium within the datasets. This will require low resolution scanning at organ level and then High Resolution scanning of the aortic root and valve. |
| | ii. | XPCI and MicroCT analysis of selected series of cases using the optimised protocols, covering approximately 30-50 specimens. |
| | iii. | Segmentation of imaging datasets into differing tissue components as described above as well as definition of surrounding microvasculature. |
| | iv. | Shape & computational analysis of the systemic outflow tract in the specific forms of CHD described above, including valvar morphology, muscular/fibrous support and adjacent valvar and conduction tissue structures in terms of possible surgical repair or device design. |
| Workpackage 4 | i. | Review and long-term follow-up of patients with systemic outflow tract repair at GOSH and analysis in terms of imaging and type of surgical repair. Interpretation of these results in terms of new information gained from micro-anatomical analyses. |
Skills to be achieved by the PhD trainee:

The end of the degree the PhD student will have obtained the most detailed knowledge of the left ventricular outflow tract in these specific forms of CHD that is currently possible. They will gain specific experience in XPCI, MCT imaging, in computational image analysis and reconstructions and have related this to the clinical experience of imaging and surgical repair at GOSH. This should put them in an excellent position to continue their surgical training putting this information into practice, inform on device design, and perhaps explore hybrid ‘surgical/interventional’ areas of Cardiothoracic Surgery.

Relevance to the area of paediatric surgery:

The end of the degree the PhD student will have obtained the most detailed knowledge of the left ventricular outflow tract in these specific forms of CHD that is currently possible. They will gain specific experience in XPCI, MCT imaging, in computational image analysis and reconstructions and have related this to the clinical experience of imaging and surgical repair at GOSH. This should put them in an excellent position to continue their surgical training putting this information into practice, inform on device design, and perhaps explore hybrid ‘surgical/interventional’ areas of Cardiothoracic Surgery.

References:


